



Operation: Present and Future

<http://protein.nsls.bnl.gov>



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Mission

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The East Coast NIGMS Structural Biology Facility mission is to provide first class resources to the biological- biochemical-, and biophysics- communities to explore all aspects of structural biology. It is the goal of this facility to provide assistance to expert and non-expert crystallographers.

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These goals include:

- Beam line access to a structural biology community at large.
- Fast access to beam time for the user community.
- Crystal screening and high-throughput data collection.
- Assistance and training for academic and professional users.

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Background



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NIGMS Initiative in 1999*

- Beamline upgrades for benefit of general users
- Reports on increasing demand for user access and beamline needs
- Estimate of doubling of capacity for crystallographic experiments from staff increases and equipment upgrades
- Letter to synchrotron facility directors inviting informal proposals
- NIGMS synchrotron advisory group
- FY99 funding of \$7M from NIGMS

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* source Norvell, Aug1999



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The NIGMS support at the NSLS

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- construction of bending magnet beamline
- including beamline optics, monochromator, detector, crystallography station
- four beamline scientists/technicians
- \$2,372K equipment/construction
- \$670K annual – staff and operation

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Facility Resources

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Optical element					
	<i>crystal channel cut</i>	<i>energy range</i>	<i>band pass</i>	<i>Intensity</i>	<i>spot size</i>
monochromator	Si(111)	6 -23 keV	1.9×10^{-4}	1.2×10^{10} ph/s	$0.1 \times 0.5 \text{ mm}^2$
	coating	figure	magnification	acceptance	
mirror	Rh	Thoroidal	1:1	3mrad	

* I=230 mA, 200 μ m slits at 1.2 Å

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Experimental Station



Beamline control:

EPICS / VME

Diffractometer control:

Compumotors

Goniometer control:

Galil

Automounter:

Wago

In line sample viewer:

Wago

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Experimental Control, Data Analysis and Storage

Experiment control	1TB RAID 10 system, Dual AMD Opteron 242 Dual Gigabit network
Data Analysis	twin RAID 10 system
Data Analysis - Firewall	130GB SCSI Dual Athlon MP
Backup - Long Term Storage; Data Analysis:	1TB RAID 5 system, Dual AMD Opteron 248 Dual Gigabit network

Data Collection	BluIce/DCS
Data Processing	HKL2000, MOSFLM
Data Analysis and Refinement	ShelX, CCP4, SOLVE, RESOLVE, CNS,etc
Model Building	Coot, O

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Crystallization Laboratory

User support:

- Crystallization
- Sample handling
- Cryogenics



Equipment

- ❖ Akta Explorer 10 for purification
- ❖ Centrifuges
- ❖ UV spectrometer
- ❖ Fast Gel-system
- ❖ Incubators for controlled temperature crystallization
- ❖ pH meters, balances



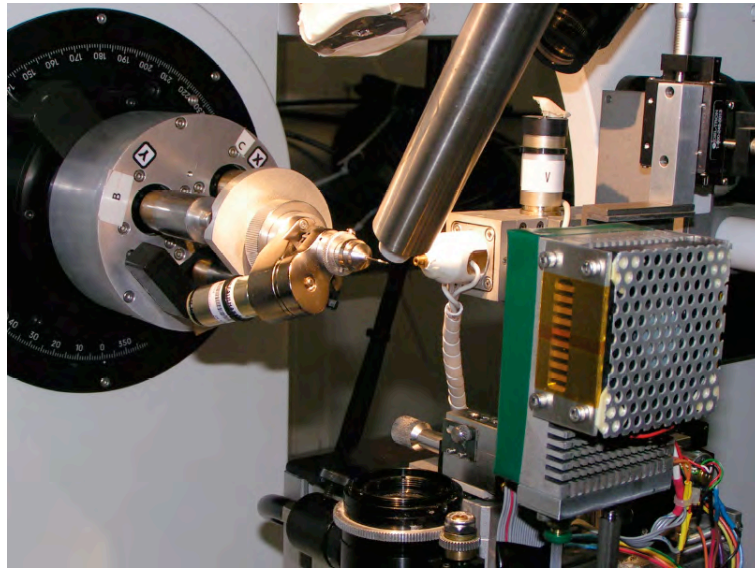
Technical Developments



Hardware

- Fluorescence Detector - NSLS
- Beam Position Monitor - NSLS
- Sample in line viewer - ALS design
- Sample Illumination - NSLS

Fluorescence Detector - NSLS design

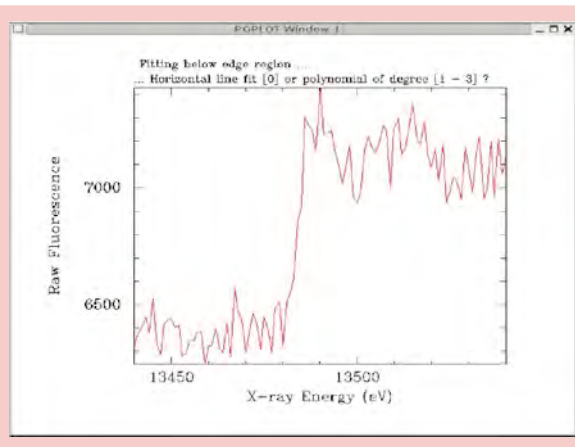


32 element solid state detector

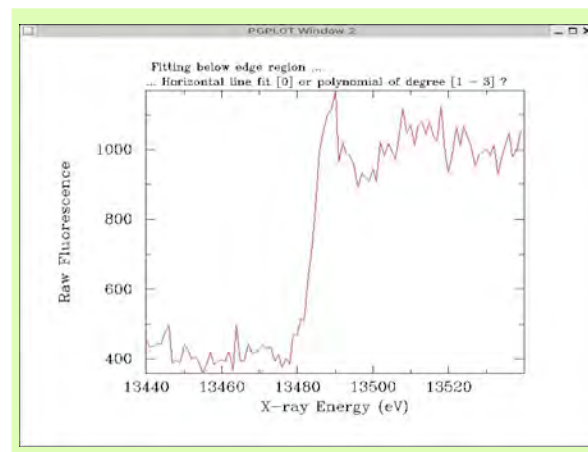
Reasons for replacement of the scintillation detector:

- Improved energy resolution, ~ 220 eV, ~ 25 eRMS

Improve the measurements of small fluorescence signals



1mg/ml Br solution on a 0.2 mm loop



Current Status:
➤ available

NSLS Control and Detector Group
D. P. Siddons, A. Kuczewski

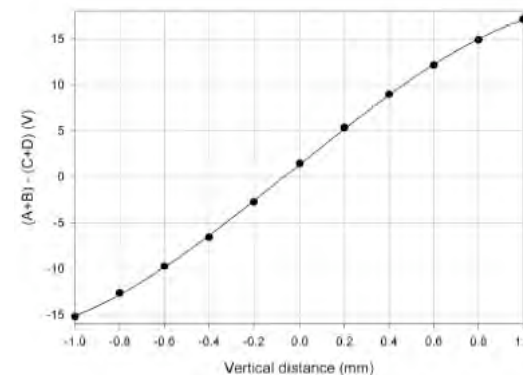
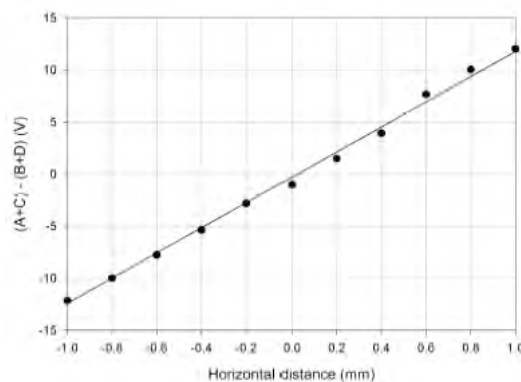
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Beam position Monitor - NSLS design



Beam Position Monitor:

- Replaces Ion Chamber
- Resolution ~2 microns

Current Status:

- available

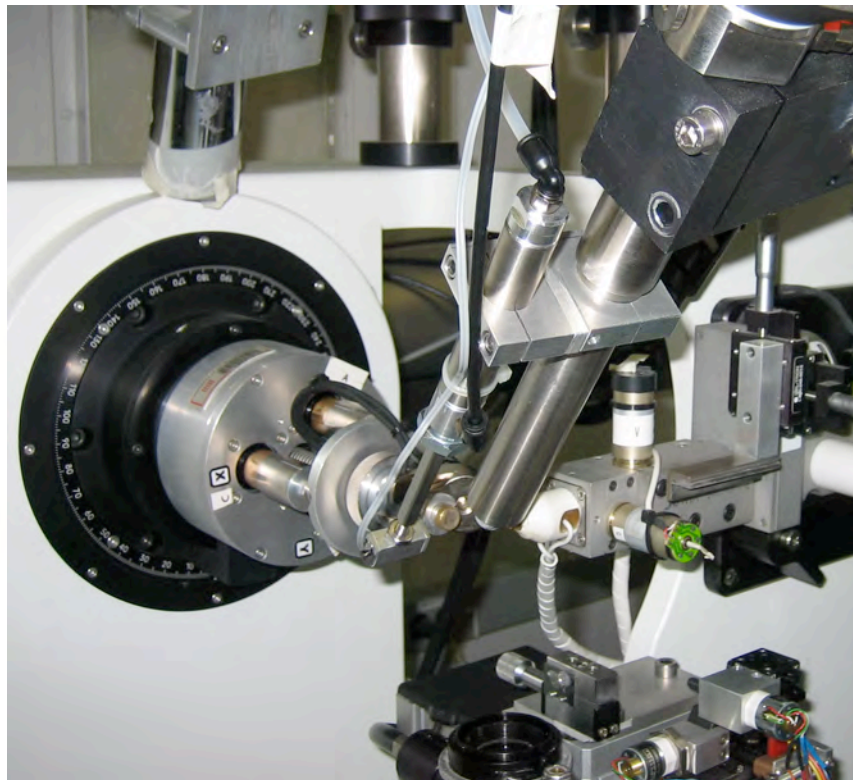
NSLS Control and Detector Group
D. P. Siddons, A. Kuczewski

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In Line Sample Illumination - NSLS design



Improved Sample Illumination:

- Improved contrast
- Automated crystal centering

Current Status:

- available

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NSLS Control and Detector Group
D. P. Siddons, A. Kuczewski
NSLS Operation group
T. Lenhard

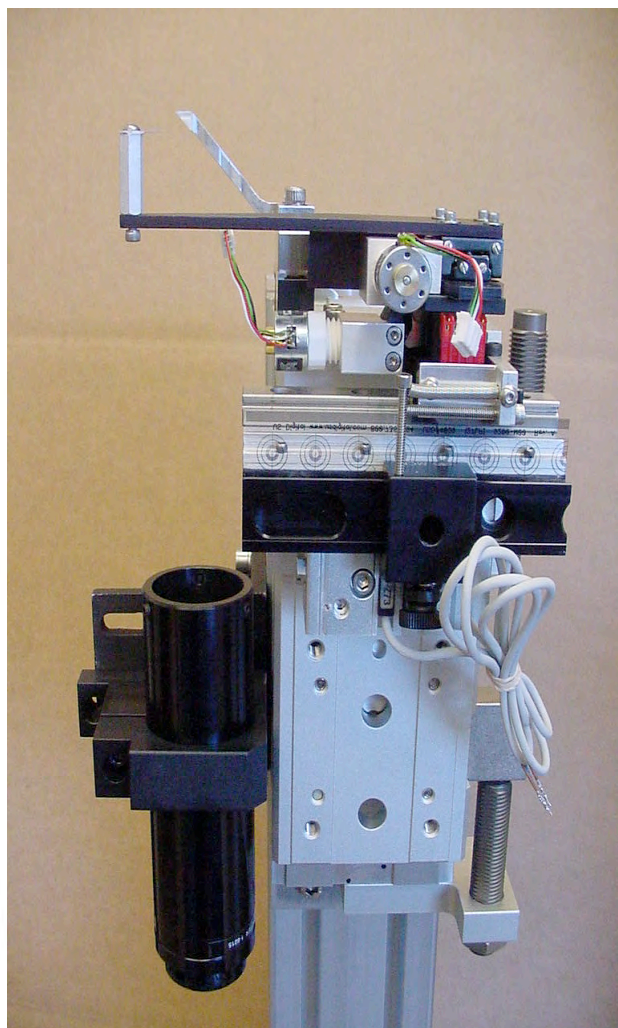
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Sample in line viewer - ALS design



Reasons for an in-line viewer:

- Sample viewing major complain
- Automated crystal centering

Implementation Strategy:

- Build by the ALS Bio-Instrumentation
- Control software compatible with Blu-Ice like Graphical User Interface/ Distributed Control System

Current Status:

- restricted
- needs to be upgraded

ALS Bioinstrumentation Group
T. Earnest, E. Cornell, R. Nordmeyer, D. Yoder

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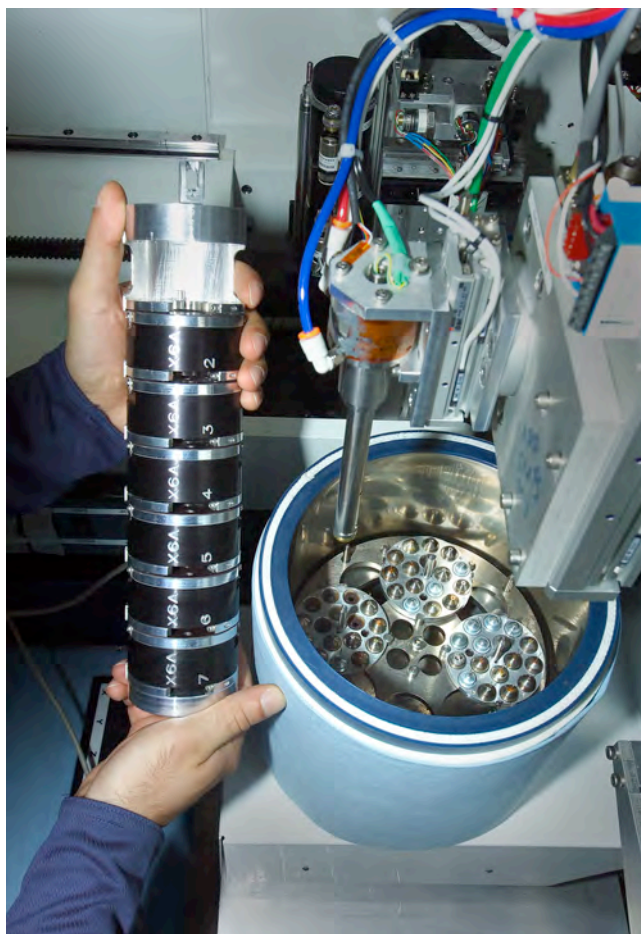
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Automated Sample Mounter - ALS design



ALS Bioinstrumentation Group
T. Earnest, E. Cornell, R. Nordmeyer

1500 crystals screened!

- ~10 groups
- 200 datasets
- ~ 30 structures in the works

Failures between 1 and 3%!

Main Causes:

- Eager users ->
command “overload”
- Failure to introduce warm up
cycles to the gripper
- Magnet base too strong
- Badly positioned samples in the pucks

Current Status:

- Operational

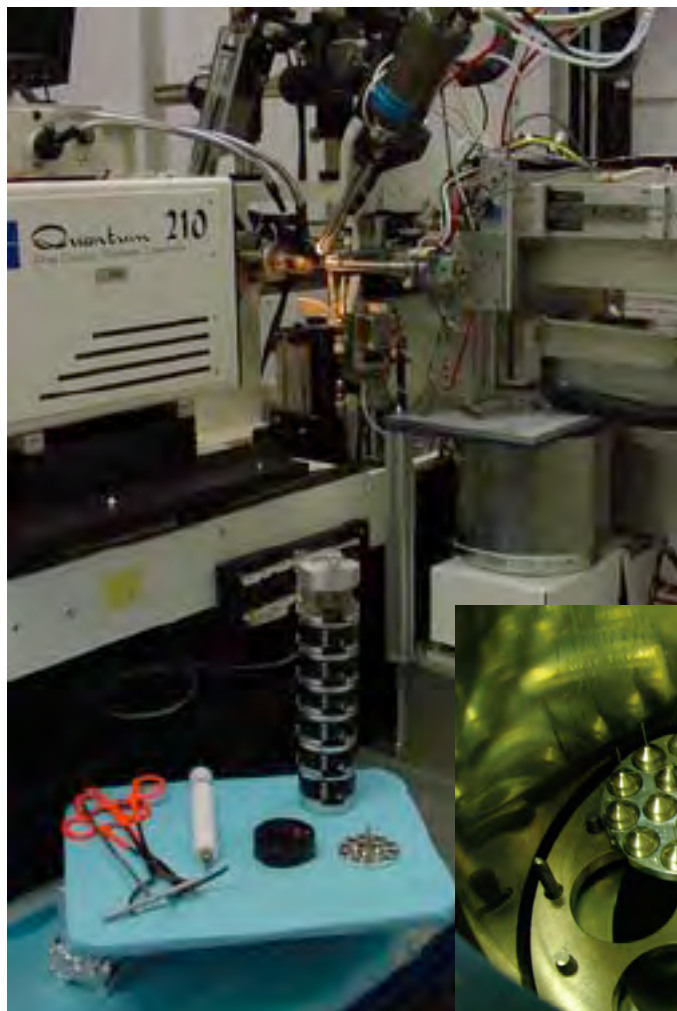
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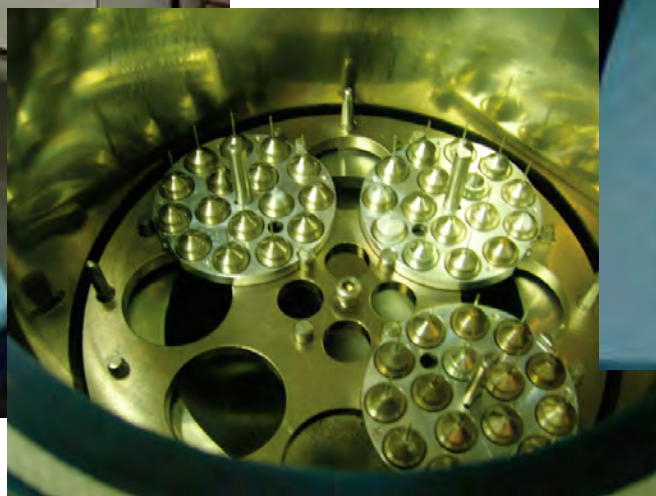
Automated Sample Mounter - ALS design



Two tool sets for users to borrow.
Two MOVIES to watch!

Requirements:

- will send set (tools + dewar) one week prior to beam time
- set has to be back one week after beam time



Current Status:

- Operational



Software

- Blulce / DCS
- CrysCent
- Crysis

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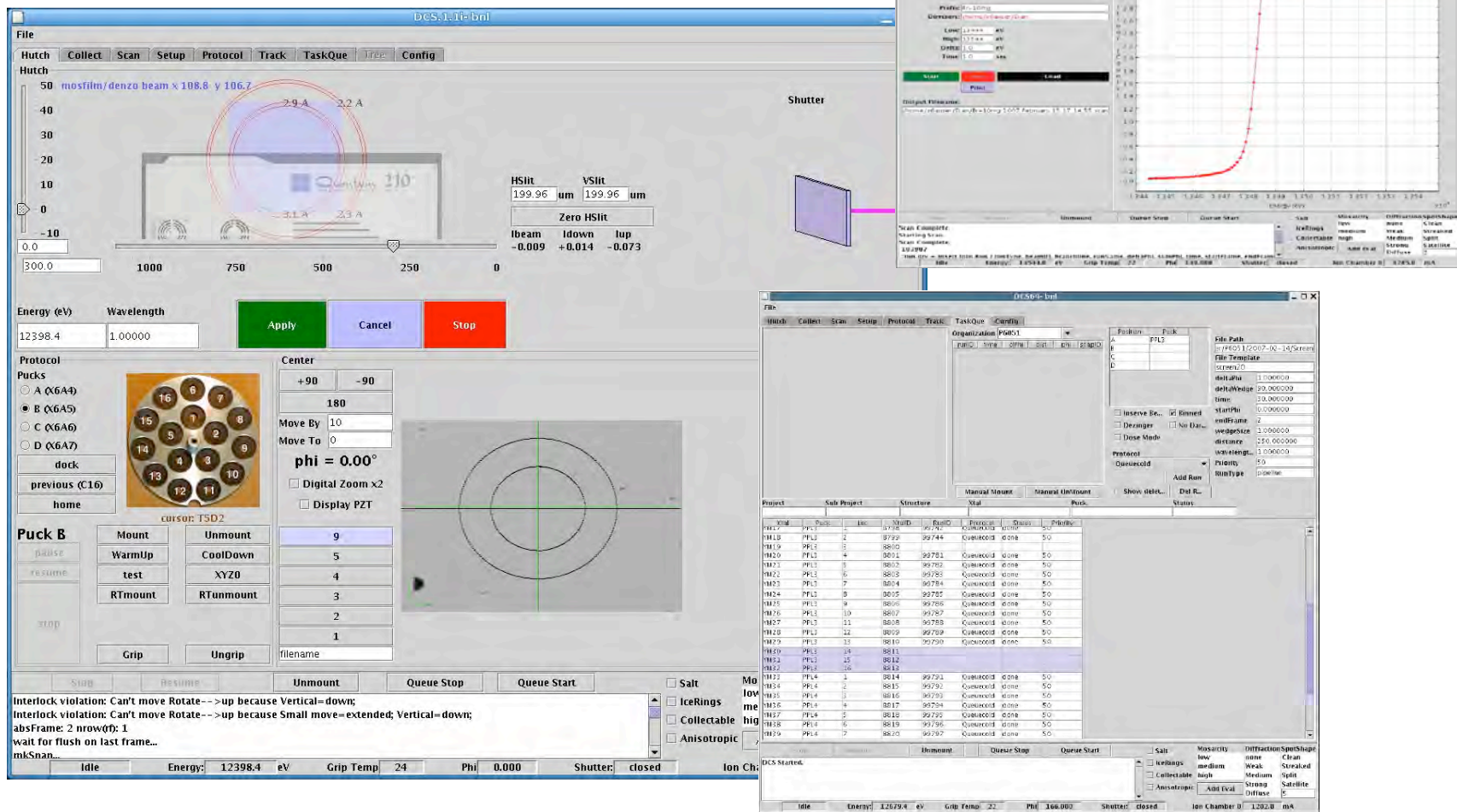
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BluIce/DCS - Experimental control

Need to be Beam Line Specific!



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Blulce/DCS - Experimental control

Need to be Beam Line Specific!

- Energy scans
- TaskQue
- Smaller Implementations
 - Beam sense
 - Slit adjustment

Key to developments:

- Assistance from Detector and Control Group
- Assistance from Earl Cornell, LBL
- Collaboration with Takeda San Diego Scientists

Current Status:

- Operational

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CrysCent

Goal: is full automation of the crystal centering process

Follows a “human” Protocol

- Uses machine vision and image processing techniques
- Is Platform-independent
- Zero-click, fully automatic crystal centering



Current Status:

- Operational

Future Tests:

- GM/CA CAT

Anubhav Jain, Cornell University SULI Program, DOE
Submitted

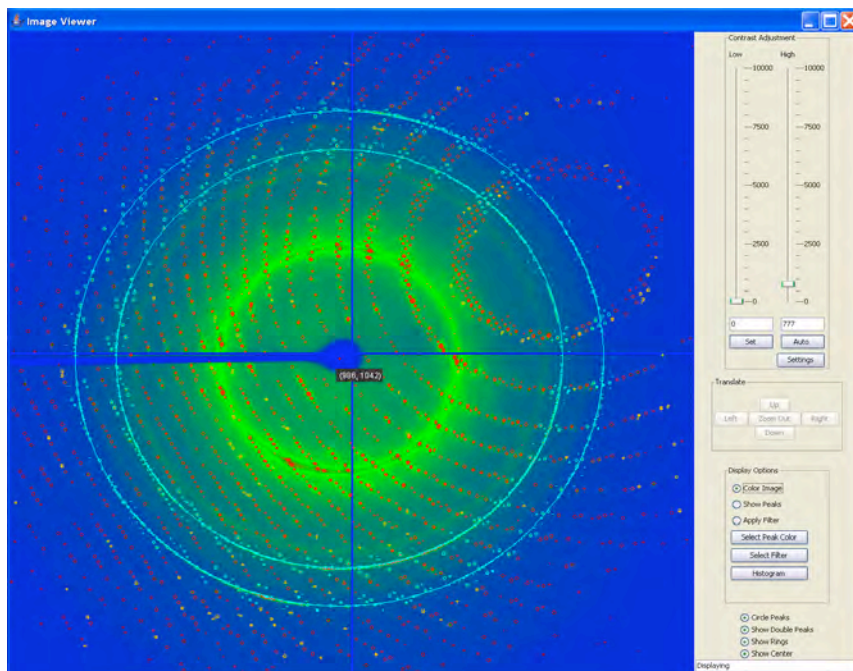
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CrySis

CrySis (Crystal Analysis) is a software designed to serve as an automated quality control tool for protein crystallography diffraction patterns.



Typical example of Crysis GUI. Shown diffraction peak finding and resolution limit determination screen

Alec Berntson, Cornell University SULI Program, DOE

CrySis

- Is based on Neural Network algorithms.
- Uses machine vision and image processing techniques
- Is Platform-independent
- Allows for automated crystal and diffraction quality assessment.

Current Status:

- Alec's CS Master Thesis!

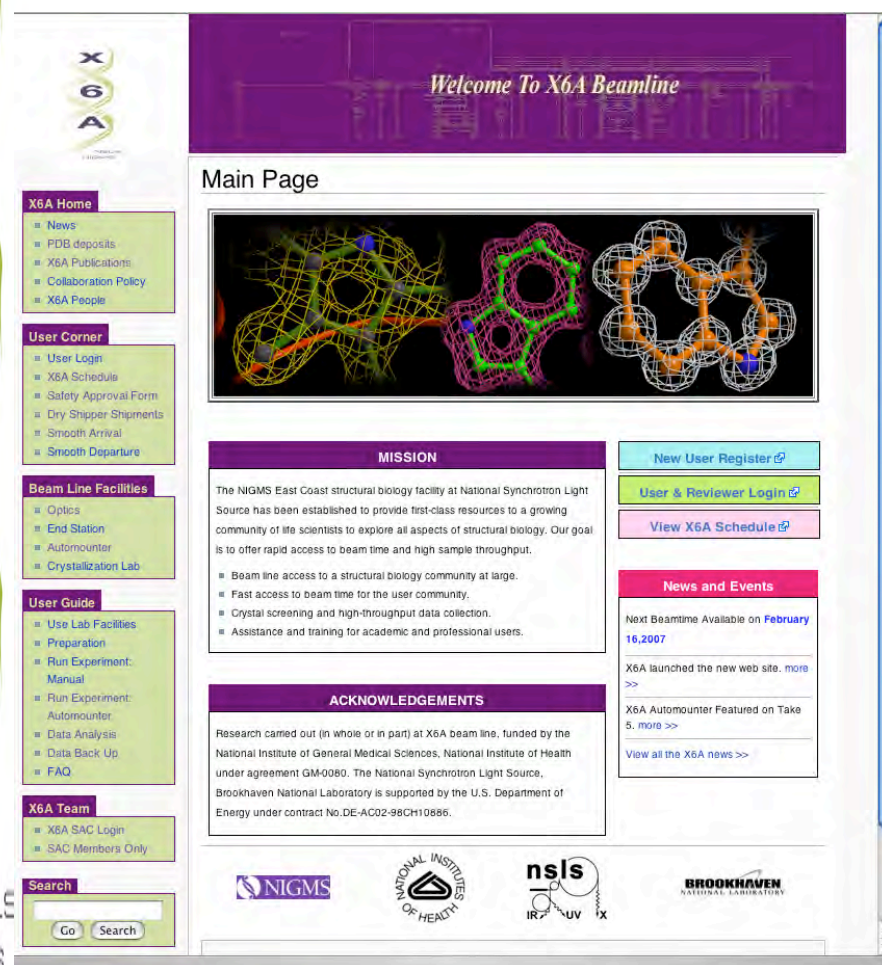
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The X6A Web and Database environment



Re-Designed!

Media Wiki

➤ Improve communication

User and Experimental Control Databases

➤ Communication between databases

User Database

➤ Improve User Access
 ➤ Improve Beam Line Management
 ➤ Real time Statistical Analysis of beam time usage

The X6A Web and Data Base environment

Scier

Path	createDate
c:\User\X6969\2007-02-16\Collect\4d3-1	2007-02-17 23:09:5
c:\User\X6969\2007-02-16\Screen	2007-02-17 21:56:4
c:\User\X6969\2007-02-16\Collect\4c4-3	2007-02-17 20:42:0
c:\User\X6969\2007-02-16\Screen	2007-02-17 18:28:0
c:\User\X6969\2007-02-16\Screen	2007-02-17 18:15:2
c:\User\X6969\2007-02-16\Collect\4c4-1	2007-02-17 16:53:1
c:\User\X6969\2007-02-16\Screen	2007-02-17 14:33:0



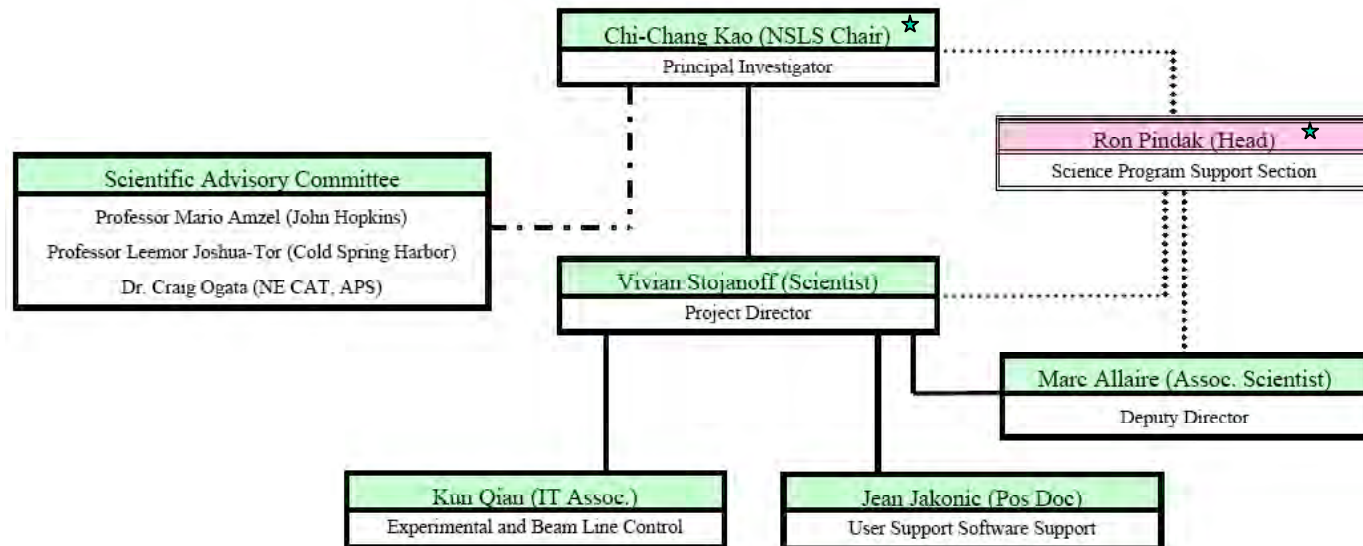
Staff

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Staffing



* NSLS scientific staff

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NSLS Staff contributing to the operation

Technical support provide by the NSLS as needed

Peter Siddons Controls&Detectors

(B. Clay, I. So, Z. Yin, T. Kuczewski)

Steve Hulbert Beamline Support

(S. Cheung, R. Greene, T. Lenhard)

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Administrative support provide by the NSLS as needed

Brian Boyle

Budget Administration

(W. Morrin)

Eileen Morello

Secretarial Support

(A. Bowden)

Katheleen Nasters

User Administration

(G. Cisco, L. Flyn, M. Baez)

A. Ackerman

EH&S

(J. Aloï)

E. Johnson

Operation and Control

B. Kiss

Building Management

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User Program



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Beam Time Access

Two modes are available to users for beam time application:

➤ Program Proposal

- ❖ General User Proposals submitted through the PASS system
- ❖ Multiple projects in one single proposal

➤ X6A Fast Access (<http://protein.nsls.bnl.gov>)

- ❖ Projects submitted through the X6A application form
- ❖ Single Projects (1Protein = 1Project)
- ❖ Easy, simple and fast (3 days to a week review process)
- ❖ Multiple visits
- ❖ User schedules own beam time

❖ **Current Status:**

➤ Operational

- ❖ Crystal Form Excel spread sheet template to account for automounter operation
- ❖ Integration to the Data Collection Software

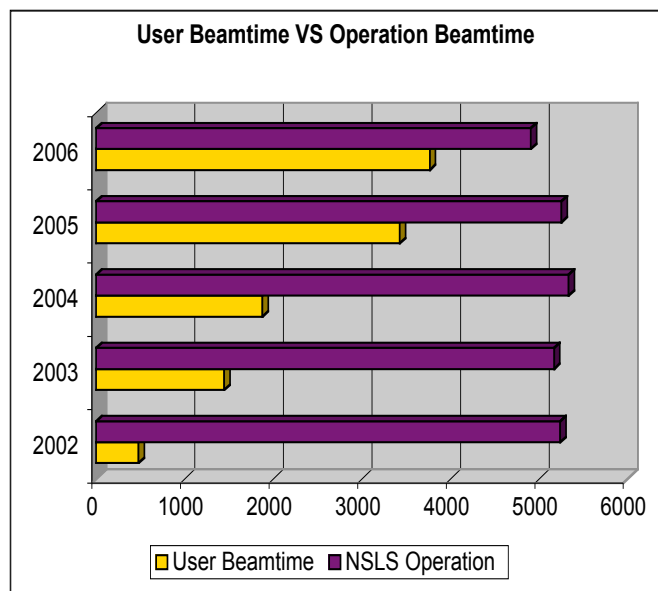
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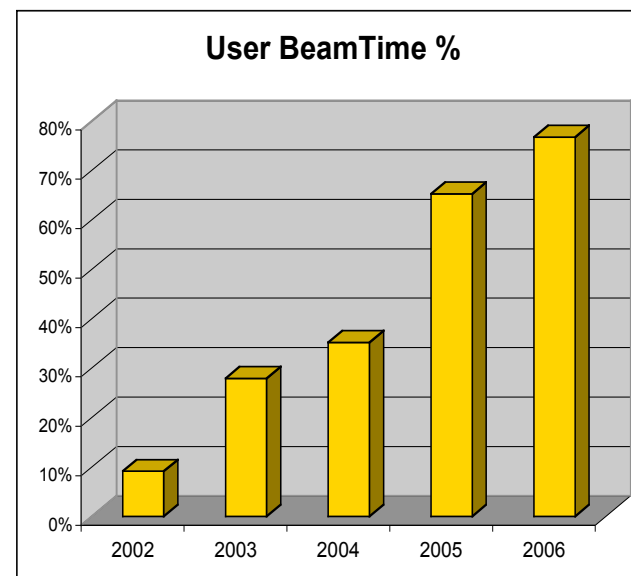
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X6A Operation: Available Beam



Steady increase in user scheduled beam time reaching saturation

Fully subscribed as 102% of the beam time available to users has been scheduled in 2006.



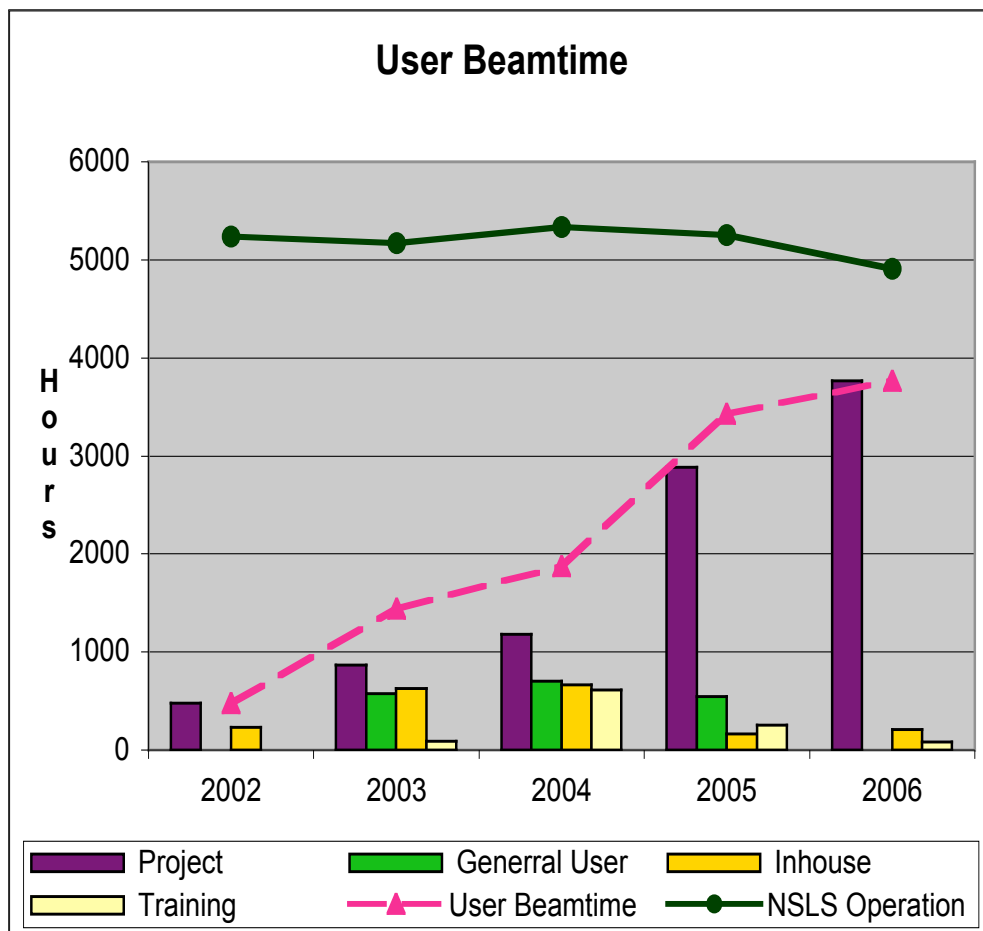
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User Beam Time



Only one Training Project
in calendar year 2006!

X6A was host to Case
Center for Proteomics
macromolecular users:

18% of NSLS operations

➤ used 38%

➤ reverted to X6A 62%

✓ Inhouse (18%)

✓ X6A user program
(60%)

✓ Unused (22%)



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Exploring the future: a new type of User

Virtual Users

- Not present during the measurement
- Typically a Fast Access project
- Send in their samples
- Receive image files and scaled data
- Usually also receive an electron density map

Are required to have visited at least once

- ~ 7 groups sending the samples
- ~ 6 leaving samples behind

Some were automounter users!

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Exploring the future: a new type of User

Remote Users

- Not physically present at the facility
- Controls the experiment either assisted by local staff (Video Conferencing) or NoMachine technology with limited staff assistance

Current status: commissioning

- NoMachine free software installed and tested on beamline computers.
- Successful Data Collection during the Mid Atlantic Macromolecular Crystallography meeting

“Educational” Movie can be downloaded from our web site!

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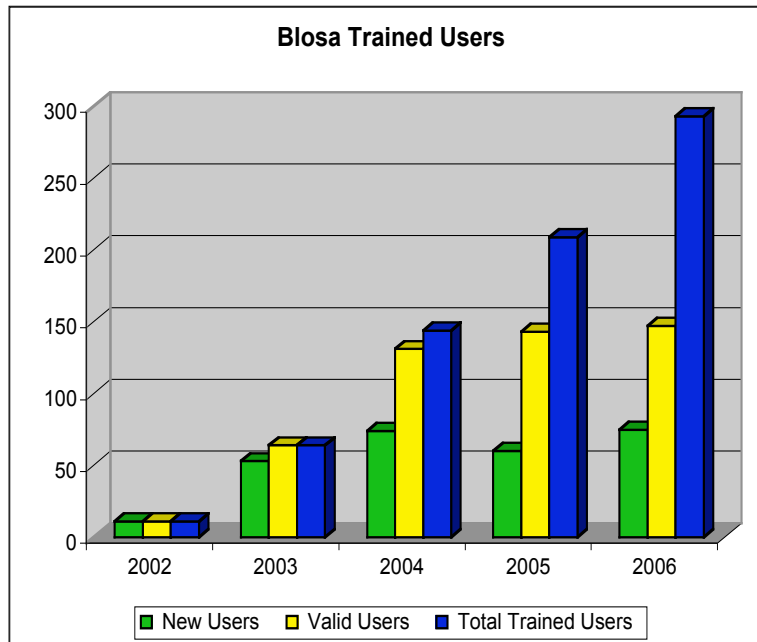
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BLOSA (Beam Line Operation and Safety Awareness) trained Users



BLOSA training is valid for two years.

**New Users*: are experimenters who got trained in a specific year and were never BLOSA trained in previous years.

**Valid Users*: are experimenters who keep a valid BLOSA Training Status in a specific year.

**Total Trained Users*: are experimenters who trained in that year or before (accumulated number). Numbers include new and returning users.

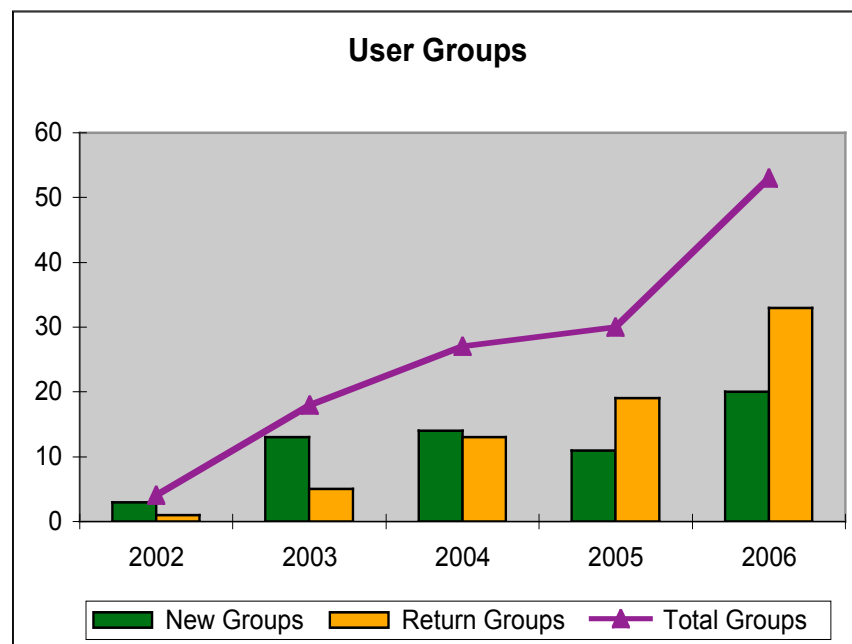
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Consolidation of the user community*



The number of users returning to the beam line has increased significantly in 2006 with 33 returning users and 20 new user groups.

*Source X6A Survey December 2006

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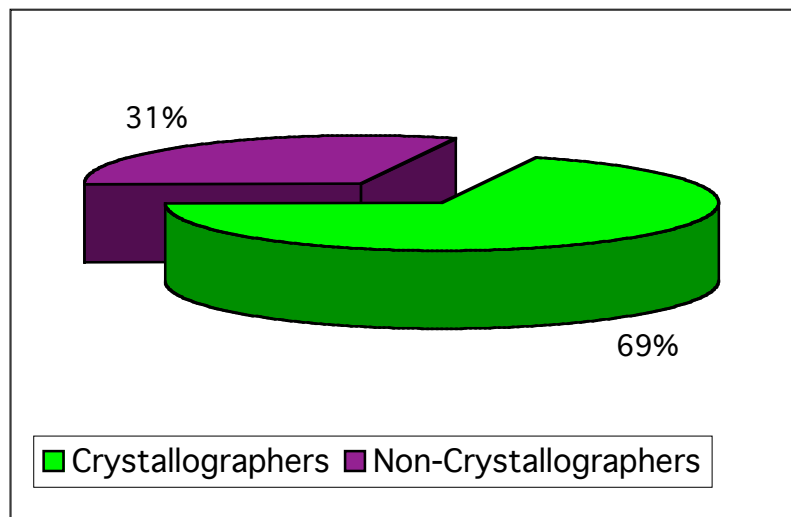
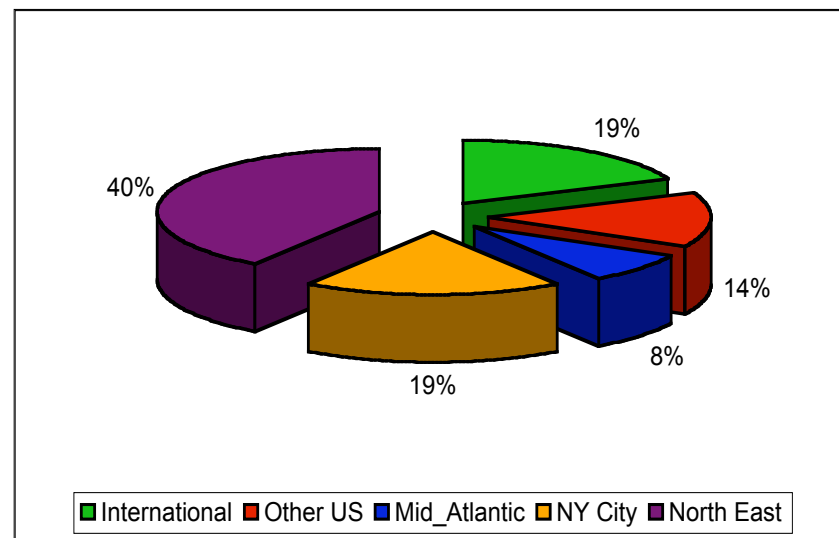
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User Group Demographics

59% of all user groups come from academic institutions located in the northeast region of the US.



Expert and Non-Expert*
user groups.

*numbers are based on project PI's

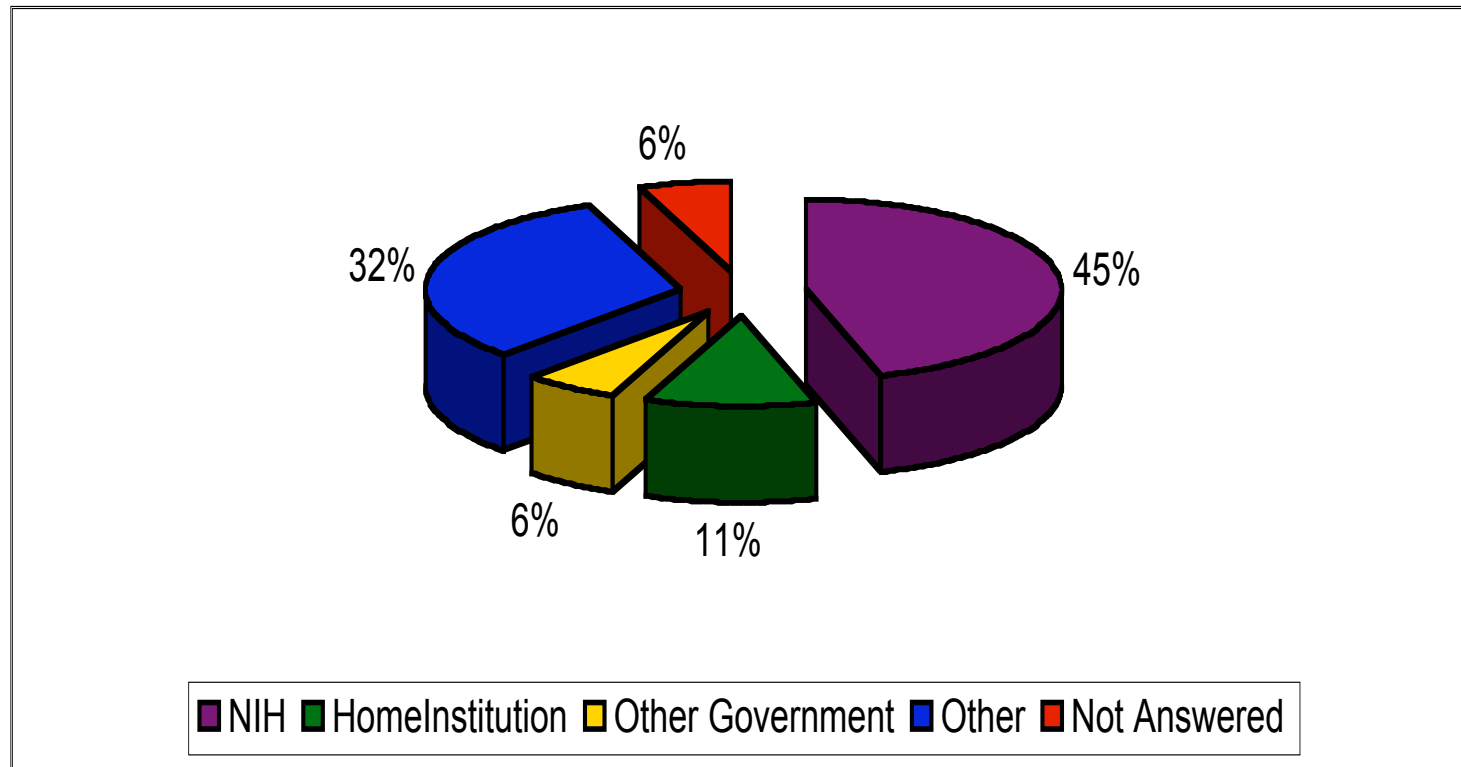
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Users Funding Sources



Number of groups supported by the NIH decreased 5% in relation to last year while funding by other sources increased. This is in direct relation to the X6A user base predominantly researchers at the beginning of their careers.



Impact

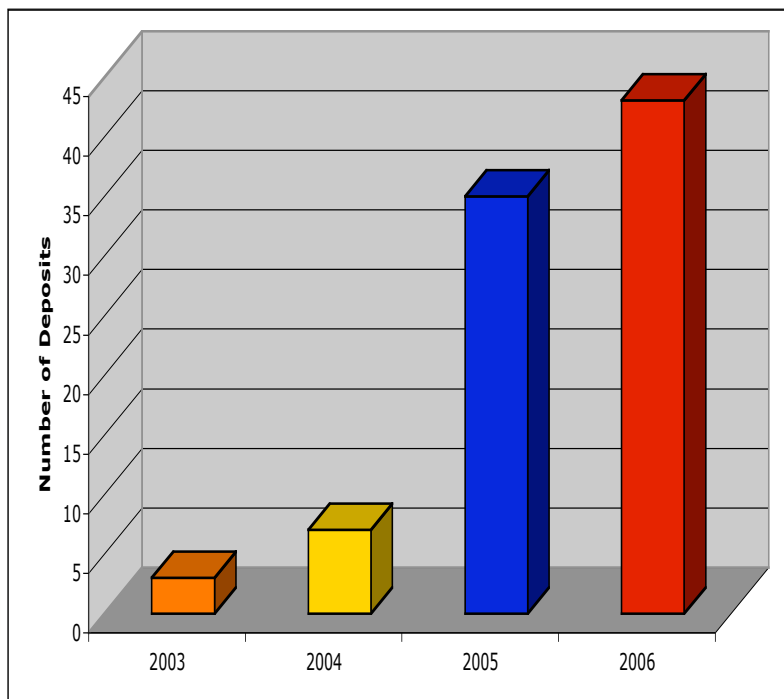
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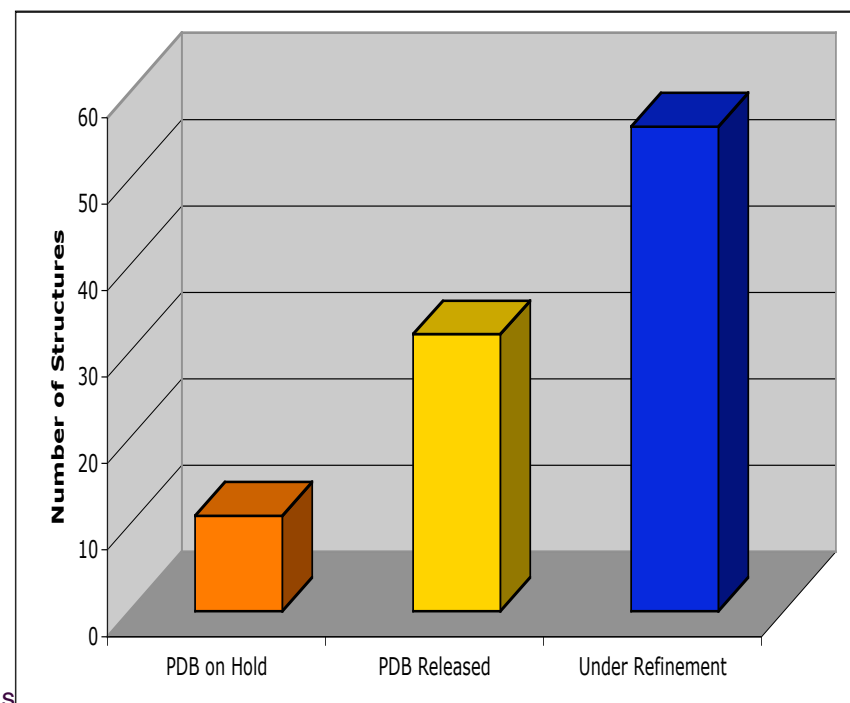
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Protein Data Bank Deposits*



Number of deposits has increased as the beam line is coming to its saturation. The total number of structures related to work performed at the beam line has nearly double in 2006.

The number of structures in refinement is larger than the structures released or on hold in 2006. It takes an average of 16 months for users to submit a PDB.



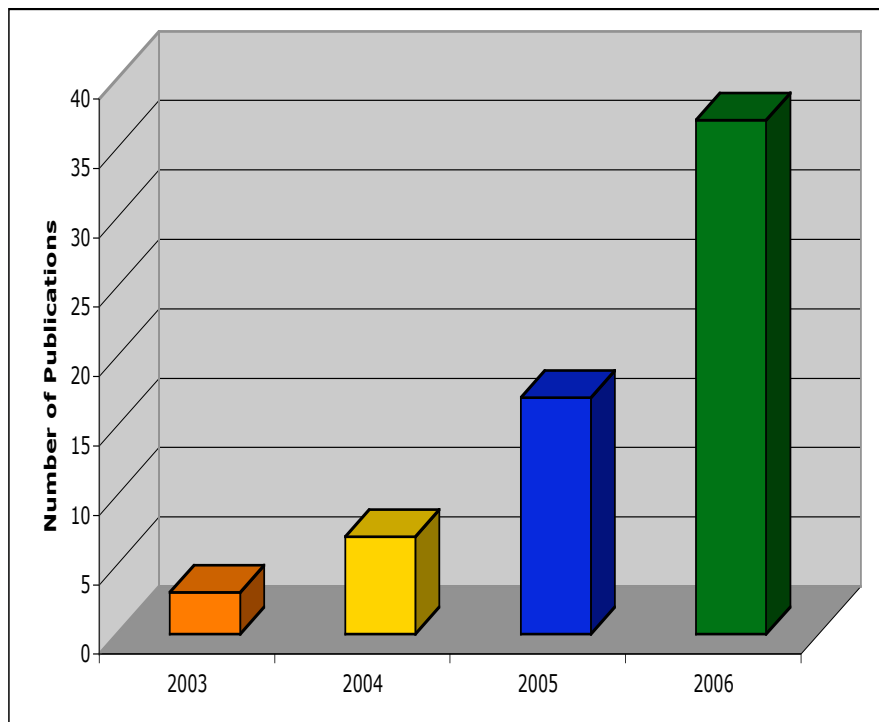
*Source X6A Survey December 2006

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Publications*



Publications	
Total	High Impact*
66	29
2006	
37	14

* Journals with an impact of six or greater

The total number of publications doubled in 2006 with X6A just coming shy of NSLS insertion device beam lines.

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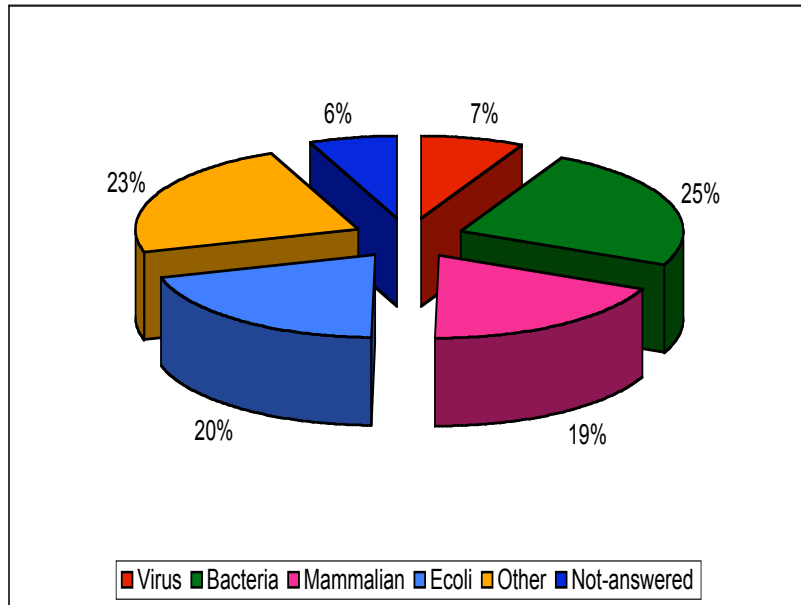
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*Source X6A Survey December 2006

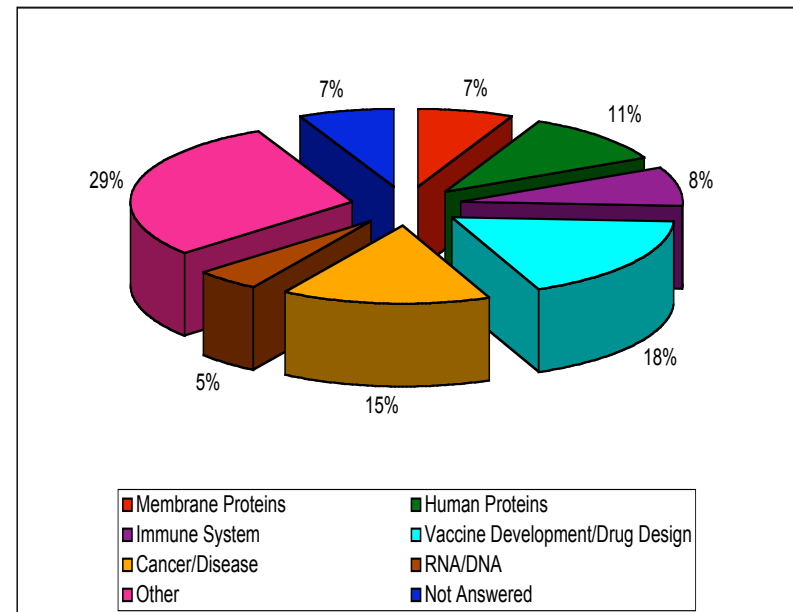
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Other Impact Indices*

Projects by Source organism



64% of the projects developed at the facility focus on topics considered particularly challenging by the NIGMS**



Projects by Subject Area

*Source X6A Survey December 2006

**Source NIGMS FY2006 and 2007 Budget

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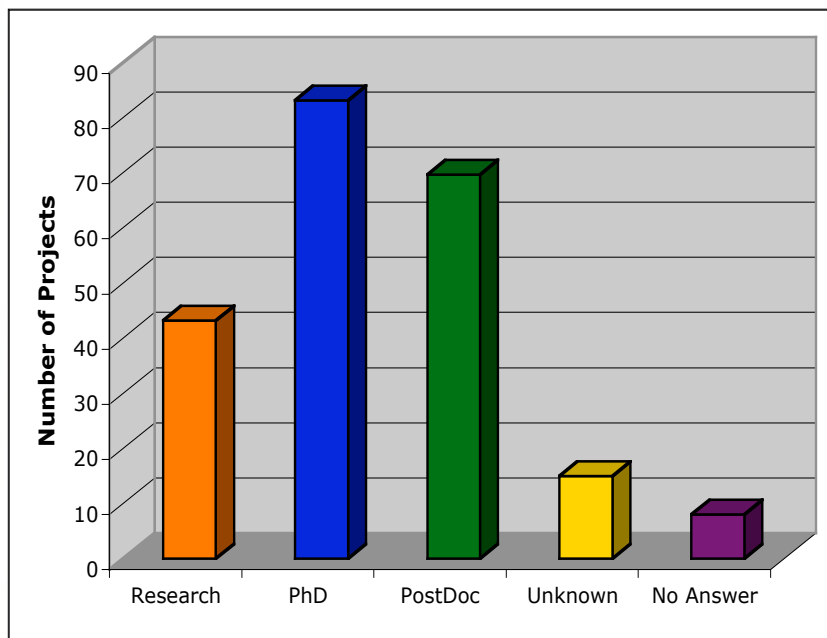
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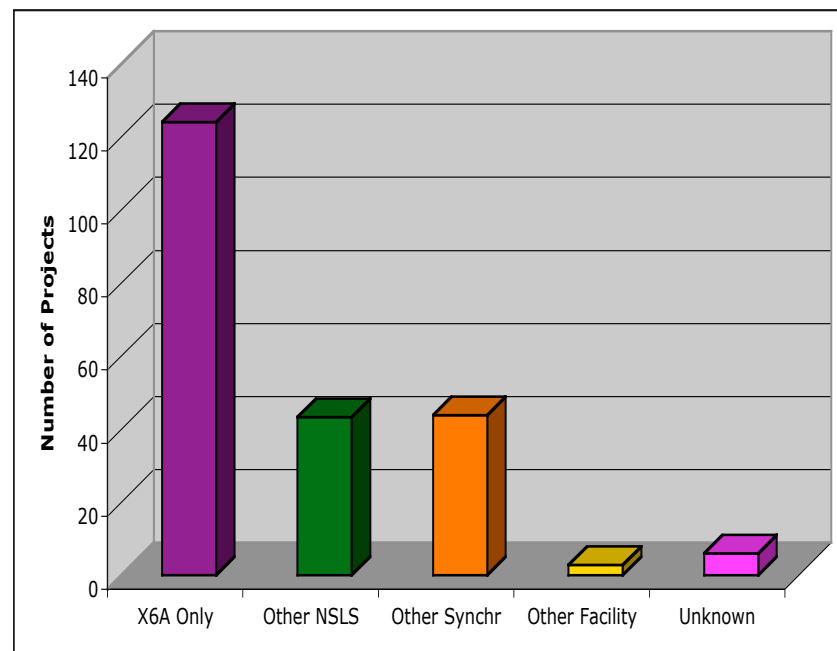
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Other Impact Indices*



70% of projects developed at the facility support the training of a scientific workforce as reflected by the numbers of PhD and Post-Doctoral research.

More than half of the projects are carried out solely at the Facility, 38% have also used other facilities and further 3% did not answer to this line item in the survey.



*Source X6A Survey December 2006
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Synergy



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Synergy

➤ NSLS

❖ X4 PRT

- User beam time re-allocation
- Technical and scientific approaches to crystallography

❖ PXRR

- X6A users in need of insertion device beam time have been allocated beam time on X29 during their X6A beam time
- Safety Approval Form - Streamline
- High pressure freezing facility

❖ Host for Case Center for Proteomics

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Synergy

With other Synchrotron Facilities

➤ *CHESS/MiTeGen*

CrysCent autocentering software

➤ *ALS*

Distributed Control System: Further developments and functionality implementations, (Thomas Earnest, Carl Cork, Earl Cornell).

Automounter feed-back: Christine Tramer (now at SSRL) ???

Sample detection interlock: Christine Tramer (now at SSRL) ???

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Synergy

With other Synchrotron Facilities

➤ SSRL

Universal puck assembly: testing the universal puck assembly with the X6A sample automounter (A. Cohen, M. Soltis)

Beam line instrumentation: where designs and instrumentation can be shared.

Software development: implementation of web-based user access functionalities; needs careful analysis.

➤ APS

CrysCent: GM/CA CAT, soft for hard - ware?

Automounter dewar: so far the best dewar seems to have been develop by SER CAT. Simulates gravity feed.

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FUTURE



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Short Term Goals: Technical developments

Improvement of the diffractometer upstream slit assembly:

- ❖ Secondary slit box and Helium path
- ❖ Upgrade of rotation axis

Automounter:

- ❖ Improved lid design
- ❖ Reliable autofill system for dewar
- ❖ Fully automated sample screening
 - Upgrade of In-line sample viewer

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Interlock sample-on and sample-in gripper:

- ❖ Sample detection on goniometer head and inside gripper
- ❖ Integration with DCS

Interlock beam stop:

- ❖ Detection of beam stop in position
- ❖ Integration with DCS

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Short Term Goals: User program

Beam Time Access:

- ❖ Provide a user friendly environment as many experimenters are first time synchrotron users;
- ❖ Consolidation of *Virtual User*, staff assisted sample automounter use;
- ❖ Encourage Remote access

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Summary

- Strong research program with good alignment with NIGMS mission.
- Young Faculty User base.
- Upgrade of Internet Services facilitates User access to beam time and Facility management.
- Inhouse development of software and beam line instrumentation increase data collection efficiency.
- Increased beam line productivity has been noticeable in 2006.
- Good synergy with other Facilities.

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